

## REMARKS

Reconsideration and allowance are respectfully requested.

Claims 10, 12-23 and 26-37 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry.

Although some of the limitations of new claims are based on claims 1 and 3-9, claims 26-35 are directed to the elected invention and should be examined in this application. Non-elected claims 1-9 and 24-25 were withdrawn by the Examiner; they are canceled without prejudice to future prosecution of that subject matter. Applicants request rejoinder of claims 22-23 and 36-37 upon allowance of an elected claim.

As an initial matter, it is noted that the Examiner's citation of PCT/JP05/04392 on page 2 of the Office Action is incorrect. This application is a U.S. national phase of PCT/EP2005/051464.

### *Claim Objections*

Claims 18 and 21 were objected to as allegedly informal. They are amended to correct the informalities as suggested by the Examiner.

Withdrawal of the objections is requested.

### *35 U.S.C. 112 – Written Description*

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). A specification need not teach, and preferably omits, what is well known in the art. See *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81, 94 (Fed. Cir. 1986).

Claims 10-21 were rejected under Section 112, first paragraph, because they allegedly contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention.” Applicants traverse because the specification teaches a representative number of species within the claimed genus.

The references discussed on pages 1-2 of Applicants’ specification indicate the high level of skill and knowledge in the prior art. For example, *Saccharomyces* mutants that are deficient in a gene involved in non-homologous recombination (NHR) (the KU70 gene) have improved targeting efficiency. *Saccharomyces* is a lower eukaryote with a distinct preference for homologous recombination (HR). In higher eukaryotes, which have a preference for NHR, mutants deficient in an NHR component (KU70) had been isolated (mammalian cells) and had a higher frequency of homology-directed repair but not increased targeted integration frequency.

Thus, in the prior art, the steering of the integration pathway to HR in eukaryotes with a preference for NHR did not result in increased targeted integration frequency.

Applicants demonstrate here that in filamentous fungi with a preference for NHR, steering of the integration pathway to HR resulted in increased targeted integration efficiency. This was demonstrated in two relatively unrelated species of filamentous fungi: i.e., *Aspergillus niger* and *Penicillium chrysogenum*.

Since the phenomenon was demonstrated in two disparate species within the claimed genus of filamentous fungi, a person skilled in the art would recognize that the phenomenon would occur in other species besides *Aspergillus niger* and *Penicillium chrysogenum*, and likely occurs in all fungal species with a preference for NHR.

Thus, Applicants submit that the effects observed by them and disclosed in this application are representative generally of filamentous fungi with a preference for NHR, as presently claimed.

The claimed invention demonstrates that steering of the integration pathway towards HR results in increased targeting efficiency. Steering through any of the many known components of the integration pathway is the technical feature that provides the solution to the problem solved: the technical tools used to demonstrate and exemplify the phenomenon are hdfA (the KU70 homologue in filamentous fungi) and hdfB (the KU80 homologue in filamentous fungi). A person skilled in the art would thus recognize

that modulation of a tool that steers the integration pathway towards HR will provide the desired effect of increased targeting efficiency. Such tools are taught by Applicants in their specification as KU70, KU80, MRE11, RAD50, RAD51, RAD52, XRS2, SIR4 and LIG4.

As of the effective filing date of the present application, a plethora of genomes of filamentous fungi were known and the homologues of KU70, KU80, MRE11, RAD50, RAD51, RAD52, XRS2, SIR4 and LIG4 were also identified by persons skilled in the art. Therefore, the person skilled in the art could use those homologues in filamentous fungi without undue experimentation. Further, since KU70 and KU80 were present in higher eukaryotes (mammalian cells) as well as lower eukaryotes (*Saccharomyces*), then should be no reasonable doubt that any specific filamentous fungi also comprise homologues of the identified components that could be used to steer an integration pathway towards HR.

Withdrawal of the written description rejection is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

#### *Conclusion*

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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